

1. (Currently Amended). A non-hemolytic cytolytic peptide having a selective cytolytic activity manifested in that it has a cytolytic activity on pathogenic cells, said pathogenic cells being cells which are non-naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic effect on red blood cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in which it manifests said cytolytic activity on pathogenic cells, said non-hemolytic cytolytic peptide being selected from the group consisting of:

- 9.
- (A) a cyclic derivative of a peptide having a net positive charge which is greater than +1, and comprising both L-amino acid residues and D-amino acid residues, or comprising only D-amino acid residues, and comprising an α -helix breaker moiety;
 - (B) a peptide comprising both L-amino acid residues and D-amino acid residues, having a net positive charge which is greater than +1, and having a sequence of amino acids such that the same amino acid sequence in which each residue is in the L-configuration is not found in nature, and cyclic derivatives thereof; and
 - (C) a random copolymer consisting of a hydrophobic, a positively charged and a D-amino acid,

with the proviso that the peptide is not that of SEQ ID

NO:1-, SEQ ID NO: 12 or SEQ ID NO: 14.

2. (Previously Amended). A cyclic peptide according to claim 1(A).

3. (Original) The cyclic peptide according to claim 2, which is a cyclic diastereomer derived from pardaxin or mellitin or from fragments thereof.

9, 4. (Original) The cyclic peptide according to claim 3, in which the net positive charge greater than +1 is due to the native amino acid composition, or is attained by neutralization of free carboxyl groups or by the addition of positively charged amino acid residues and/or positively charged chemical groups.

5. (Original) The cyclic peptide according to claim 4, which is selected from a cyclic diastereomer of pardaxin or of a fragment thereof to which Lys residues have been added to the N-terminus and/or aminoethylamino groups have been added to the C-terminus.

6 (Previously Amended). A cyclic peptide according to claim 1, selected from the group of cyclic pardaxin-derived peptides consisting of the herein designated peptides **86-88** (SEQ ID NOs: 86-88, respectively), of the sequence:

86) Cyclic $K^1[D]P^7 L^{18}L^{19}$ [1-22]-par of the sequence:

Cys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-Ser-
Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys,

87) Cyclic $K^1 K^2[D]P^7 L^{18}L^{19}$ [1-22]-par of the sequence:

Cys-Lys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-Ser-
Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys, and

88) Cyclic $K^1 K^2 K^3 [D]P^7 L^{18}L^{19}$ [1-22]-par of the sequence:

Cys-Lys-Lys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-
Ser-Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys.

9, 7. (Previously Amended). A peptide according to claim 1(B).

8. (Previously Amended). The peptide according to claim 7, having the following characteristics:

- (a) it is a non-natural synthetic peptide composed of a ratio of at least one hydrophobic amino acid and at least one positively charged amino acid, and in which sequence at least one of the amino acid residues is a D-amino acid;
- (b) the peptide has a net positive charge which is greater than +1; and
- (c) the ratio of hydrophobic to positively charged amino acids is such that the peptide is cytolytic to pathogenic cells but does not cause cytolysis of red blood cells.

9. (Previously Amended). The peptide according to claim 8, wherein the positively charged amino acid is selected from the group consisting of lysine, arginine and histidine, and the hydrophobic amino acid is selected from the group consisting of leucine, isoleucine, glycine, alanine, valine, phenylalanine, proline, tyrosine and tryptophan.

9, 10. (Previously Amended). The peptide according to claim 9, wherein the net positive charge greater than +1 is due to the amino acid composition or to the addition of positively charged chemical groups, or which hydrophobicity is decreased by the addition of polar amino acids selected from the group consisting of serine, threonine, methionine, asparagine, glutamine and cysteine.

11. (Previously Amended). The peptide according to claim 10, having at least 6 amino acid residues, in which the hydrophobic amino acid is leucine, alanine or valine, and the positively charged amino acid is lysine.

12. (Previously Amended). The peptide according to claim 11, being a diastereomer of a 6-mer, 8-mer or 12-mer peptide composed of leucine and lysine, in which at least one third of the sequence is composed of D-amino acids, but excepting the peptide herein designated 23 (SEQ ID NO:23):

23) Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-NH₂.

13. (Previously Amended). A Leu/Lys diastereomer according to claim 12, selected from the group of peptides consisting of those herein designated 24 to 29 (SEQ ID NO:24-29, respectively), of the sequence:

- 24) Lys-Leu-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Leu-Lys-NH₂,
- 25) Lys-Lys-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Lys-Lys-NH₂,
- 26) Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-NH₂,
- 27) Lys-Leu-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Leu-Lys-NH₂,
- 28) Lys-Leu-Leu-Leu-Leu-Lys, and
- 29) Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys.

g, 14. (Previously Amended). A cyclic derivative of a non-natural synthetic peptide according to claim 7, selected from the group of peptides consisting of those herein designated 92-95 (SEQ ID NOS:92-95, respectively), of the sequence: .

- 92) Cyclic Cys Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys Cys,
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- 93) Cyclic Cys Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Lys Cys,
|-----|
- 94) HN - Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys - CO, and
|-----|
- 95) HN - Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Leu Lys - CO.
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15-19. (Cancelled)

20. (Previously Amended). A non-hemolytic cytolytic random copolymer according to claim 1(C).

21. (Previously Amended). The non-hemolytic cytolytic random copolymer according to claim 20, consisting of lysine, leucine and D-leucine in the ratio 1:1:1, 2:1:1 or 3:1:1 (Mol).

22-26. (Cancelled)

27. (Previously Added). A composition comprising an acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit bacterial growth.

g, 28(New). A composition comprising an acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit growth of fungi.

29. (Previously Added). A composition comprising an acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit proliferation of cancer cells.

30. (Previously Added). The composition of claim 29, wherein said cancer cells are carcinoma cells.

31. (Previously Amended). A composition comprising a pharmaceutically acceptable carrier and a peptide according to claim 1 in an anti-viral effective amount.

32. (Previously Amended). The composition of claim 31, wherein said antiviral effective amount is an amount effective to inhibit viral-induced hemolysis.

33. (Previously Amended). A composition comprising a pharmaceutically acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit growth of a protozoan.

9, 34. (Previously Amended). A mixture consisting of two or more non-hemolytic cytolytic peptides or cyclic derivatives thereof, each peptide or derivative having a net positive charge which is greater than +1 and comprising both L-amino acid residues, and D-amino acid residues, or comprising only D-amino acid residues and comprising an α -helix breaker moiety.

35. (Previously Amended). The mixture of claim 34, wherein each peptide or derivative present in the mixture consists of 12 amino acids, each of which is selected from the group consisting of L-Leu, D-Leu, L-Lys, and D-Lys.

36. (Cancelled)

37. (Previously Added). The mixture according to claim 35, comprising a mixture of Lys/Leu 12-mer peptide diastereomers.
